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In re Application of

Application Number

07/975,750

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1. ☐ I hereby request access under 37 CFR 1.14(e)(2) to the application file record of the above-identified ABANDONED Application, which is not within the file jacket of a pending Continued Prosecution Application (CPA) (37 CFR 1.53(d)) and is: (CHECK ONE)

☐ (A) referred to in:

United States Patent Application Publication No. _____, page _____, line _____,

United States Patent Number 6,177,401, column _____, line _____, or

an International Application which was filed on or after November 29, 2000 and which

designates the United States, WIPO Pub. No. _____, page _____, line _____.

☐ (B) referred to in an application that is open to public inspection as set forth in 37 CFR 1.11(b) or

1.14(e)(2)(i), i.e., Application No. _____, paper No. _____, page _____, line _____.

2. ☐ I hereby request access under 37 CFR 1.14(e)(1) to an application in which the applicant has filed an authorization to lay open the complete application to the public.

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US006177401B1

(12) **United States Patent**
Ullrich et al.

(10) **Patent No.:** US 6,177,401 B1
(45) **Date of Patent:** Jan. 23, 2001

(54) **USE OF ORGANIC COMPOUNDS FOR THE INHIBITION OF FLK-1 MEDIATED VASCULOGENESIS AND ANGIOGENESIS**

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(73) **Assignee:** Max-Planck-Gesellschaft zur Förderung der Wissenschaften, Martinsried (DE)

(*) **Notice:** Under 35 U.S.C. 154(b), the term of this patent shall be extended for 0 days.

(21) **Appl. No.:** 08/193,829

(22) **Filed:** Feb. 9, 1994

Related U.S. Application Data

(63) Continuation-in-part of application No. 08/038,596, filed on Mar. 26, 1993, now abandoned, which is a continuation-in-part of application No. 07/975,750, filed on Nov. 13, 1992, now abandoned.

(51) **Int. Cl.⁷** A61K 31/00

(52) **U.S. Cl.** 514/1; 435/7.2; 436/501; 530/350; 530/399

(58) **Field of Search** 536/23.5; 435/69.1, 435/172.1, 240.2, 252.3, 320.1, 325, 361, 7.2; 424/93.2; 514/44, 1; 935/32, 57, 70, 71; 436/501; 530/399, 350

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(57) **ABSTRACT**

The present invention relates to the use of proteins, peptides and organic molecules capable of modulating Flk-1 receptor signal transduction in order to inhibit or promote angiogenesis and vasculogenesis. The invention is based, in part, on the demonstration that Flk-1 tyrosine kinase receptor expression is associated with endothelial cells and the identification of vascular endothelial growth factor (VEGF) as the high affinity ligand of Flk-1. These results indicate a major role for Flk-1 in the signaling system during vasculogenesis and angiogenesis. Engineering of host cells that express Flk-1 and the uses of expressed Flk-1 to evaluate and screen for drugs and analogs of VEGF involved in Flk-1 modulation by either agonist or antagonist activities is described.

The invention also relates to the use of FLK-1 ligands, including VEGF agonists and antagonists, in the treatment of disorders, including cancer, by modulating vasculogenesis and angiogenesis.

16 Claims, 25 Drawing Sheets